REMARKS

Claim Status

Claims 1-17 are pending in the application, of which Claims 15-17 are withdrawn as the result of a Restriction Requirement. Herein, Applicants amend Claims 1, 3, 5, 8, 10, and 12; cancel Claims 4, 6, 11, 13, and 15-17; and add no Claims; WHEREUPON Claims 1-3, 5, 7-10, 12, and 14 remain to be examined. No additional claims fee is believed to be due.

Claims 1 and 8 are amended to particularly point out and distinctly claim the subject matter Applicants regard as their invention by providing the full definition for "HPTPbeta", "VEGFR2", and "Tie-2", where they appear. Claims 1 and 8 are also amended to particularly point out and distinctly claim the subject matter Applicants regard as their invention by further indicating what the angiogenesis mediated disorders are selected from, for which basis lies, at least, at page 10, lines 1-3, of the specification as originally filed. Claims 1 and 8 are also amended to particularly point out and distinctly claim the subject matter Applicants regard as their invention by further indicating preferred embodiments of the amino acid sequences and their degree of homology, for which basis lies, at least, at original Claims 4 and 13, and at page 8, lines 29-31, of the specification as originally filed.

Claims 3 and 10 are amended to particularly point out and distinctly claim the subject matter Applicants regard as their invention by further indicating preferred embodiments of the amino acid sequences and their degree of homology, for which basis lies, at least, at page 8, lines 29-31, of the specification as originally filed.

Claims 5 and 12 are amended to correct dependency in view of other amendments presented herein.

Claims 4, 6, 11, 13, and 15-17 are canceled without prejudice.

It is believed these changes do not involve any introduction of new matter. Consequently, entry of these changes is believed to be in order and is respectfully requested.

Amendments to the Specification

The specification is amended to properly use trademarks at pages 25, and 27-28.

The specification is amended at pages 23 and 25 to comply with the sequence disclosure rules by inserting SEQ ID NOs where appropriate.

It is believed these changes do not involve any introduction of new matter. Consequently, entry of these changes is believed to be in order and is respectfully requested.

Formal Matters

The Examiner objects to the Specification, indicating that trademarks are not properly used, citing page 25, lines 17 and 19, and page 28, lines 10-11, and 18.

By the amendments presented herein, Applicants amend the Specification at pages 25, and 27-28, by capitalizing trademarks, identifying them with the superscript "TM", and including a brief generic description (obtained from the respective manufacturer's published materials). As such, the objection is believed to be obviated, and Applicants respectfully request it be withdrawn.

The Examiner objects to the Specification, indicating that SEQ ID NOs need to be inserted each time the phrases "HPTPbeta catalytic domain", "VEGFR2", and "Tie-2 kinase domain" appear in the specification or claims, a SEQ ID NO should follow the phrase, further indicating that such phrases occur at page 23, lines 1 and 22, and page 25, line 16, of the Specification.

By the amendments presented herein, Applicants amend the Specification by inserting SEQ ID NOs where the phrases "HPTPbeta catalytic domain", "VEGFR2", and "Tie-2 kinase domain" refer to specific sequences. As such, the objection is believed to be obviated, and Applicants respectfully request it be withdrawn.

Alleged Indefinitess

Claims 1-14 are rejected under 35 USC §112, 2nd paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter Applicants regard as their invention. Applicants respectfully traverse the rejection as applied to the amended claims as presented herein for the reasons set forth below.

The Examiner asserts that the phrase "treating an angiogenesis mediated disorder" in Claim 1 is indefinite, as no specific disease, e.g. cancer, vascular disease including coronary artery disease and stroke, and diabetes related vascularization, is enumerated.

By the amendments presented herein, Applicants amend Claim 1, in pertinent part, to further define the angiogenesis mediated disorder as being "selected from: (a) disorders, diseases, and/or unwanted conditions characterized by unwanted or elevated angiogenesis; or (b) disorders, diseases, and/or unwanted conditions characterized by wanted or reduced angiogenesis". As such, the rejection is believed to be obviated, and Applicants respectfully request it be withdrawn.

The Examiner asserts that the phrases "HPTPbeta" and "VEGFR2" in Claims 1-14, and "Tie-2" in Claims 8-12, are indefinite, as abbreviations and acronyms must be defined at least once in the claims.

By the amendments presented herein, Applicants have defined each of these terms the first time they are used in each independent claim. As such, the rejection is believed to be obviated, and Applicants respectfully request it be withdrawn.

The Examiner asserts that the phrases "HPTPbeta activity", "VEGFR2 activity in Claims 1-14, and "Tie-2 activity" in Claims 8-12, are indefinite, stating that the HPTPbeta activity is presumed to be any protein tyrosine phosphatase activity, and the VEGFR2 activity and Tie-2 activity is presumed to be any protein tyrosine activity (emphasis added).

Applicants have definitely identified a protein tyrosine phosphatase, namely, HPTPbeta, not any protein tyrosine phosphatase in their claims. The Examiner cannot simply read this limitation out of the claim to support an assertion that Applicants are claiming the activity of any protein tyrosine phosphatase. Applicants renew this argument, *mutatis mutandis*, with respective to VEGFR2 activity and Tie-2 activity. As

such, the rejection is believed to be improper, and Applicants respectfully request it be withdrawn.

The Examiner asserts that the phrase "hydrolysis of phospho-ester bond of one or more natural or artificial phosphate containing compounds", in Claims 6 and 13, is indefinite.

By the amendments presented herein, Applicants have cancelled Claims 6 and 13 and have not presented any claims of substantially the same scope. As such, the rejection is believed to be moot, and Applicants respectfully request it be withdrawn.

Alleged Inadequate Written Description

Claims 1-4, 6-11, and 13-14 are rejected under 35 USC §112, 1st paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to the skilled person that the inventors, at the time of filing, had possession of the claimed invention. Applicants respectfully traverse the rejection as applied to the amended claims presented herein for the reasons set forth below.

The Examiner asserts that the specification does not sufficiently describe all of those additional representative species encompassed by a claim to "any [HPTPbeta], and VEGFR2 and Tie-2 protein kinase from any biological source including those having 80% or 90% homology to SEQ ID NO: 2, 6, and 8". By the amendments presented herein, Applicants' claim encompasses, in pertinent part, amino acid sequences of HPTPbeta having at least about 95% homology to SEQ ID NO: 2, 9, 15, or 16, amino acid sequences of VEGFR2 having at least about 95% homology to SEQ ID NO: 6 or 11, and amino acid sequences of Tie-2 having at least about 95% homology to SEQ ID NO: 8 or 13. Applicants submit that the specification adequately describes amino acid sequences having at least about 95% homology to the above enumerated SEQ ID NOs. As such, Applicants submit that the rejection, as applied to the amended claims, is improper, and Applicants respectfully request it be withdrawn.

Alleged Insufficient Enablement

Claims 1-4, 6-11, and 13-14 are rejected under 35 USC §112, 1st paragraph, as allegedly failng to comply with the enablement requirement. Applicants respectfully traverse the rejection as applied to the amended claims presented herein for the reasons set forth below.

The Examiner asserts that claims drawn to "all possible proteins which can be described as HPTPbeta, VEGFR2 or Tie-2 or having 80% or 90% homology to any of the amino acid sequences of SEQ ID NO: 2, 6, 8, 9, 11, 13, 15, and 16" are broader than the enablement provided by the specification. By the amendments presented herein, Applicants' claim encompasses, in pertinent part, amino acid sequences of HPTPbeta having at least about 95% homology to SEQ ID NO: 2, 9, 15, or 16, amino acid sequences of VEGFR2 having at least about 95% homology to SEQ ID NO: 6 or 11, and amino acid sequences of Tie-2 having at least about 95% homology to SEQ ID NO: 8 or 13. Applicants submit that the specification sufficiently enables the skilled person to carry out the invention with amino acid sequences having at least about 95% homology to the above enumerated SEQ ID NOs without engaging in undue experimentation. As such, Applicants submit that the rejection, as applied to the amended claims, is improper, and Applicants respectfully request it be withdrawn.

Alleged Obviousness over Huang in view of Thorpe

Claims 1-2, 6-9, and 13-14 are rejected under 35 USC §103(a) as allegedly being unpatentable over Huang, et al. J. Biol. Chem., vol. 274, pages 38183-88 (1999) [herein "Huang"] in view of USPN 6,342,219 [herein "Thorpe"]. Applicants respectfully traverse the rejection as applied to the amended claims presented herein for the reasons set forth below.

Huang discloses a low molecular weight, cytoplasmic protein tyrosine phosphatase, HCPTPA, which inhibits VEGF-mediated responses in cultured endothelial cells (page 38183, col. 2, para. 2). Huang also discloses that overexpression of HCPTPA inhibited angiogenesis in the rat aortic ring assay, a model of angiogenesis that has been shown to be dependent on VEGF receptor signaling (*id.*). Huang takes these two points

together, to suggest that HCPTPA may be an important negative regulator of VEGF receptor signaling and VEGF-mediated angiogenesis (page 38183, col. 2, para. 2 to page 38184, col. 1, para 1.).

Thorpe discloses antibodies that specifically inhibit VEGF binding to only one (VEGFR2) of the two VEGF receptors, stating that such antibodies effectively inhibit angiogenesis and induce tumor regression, and yet have improved safety due to their specificity (Abstract). Thorpse further discloses that binding of the VEGF dimer to the VEGF receptor is believed to induce dimerization, which in turn, causes autophosphorylation of specific tyrosine residues on the intracellular side of VEGRR2 and VEGFR1, which again in turn, leads to a signal transduction cascade, which includes activation of phospholipase Cgamma and phosphatidylinositol 3-kinase (col. 45, lines 29-37).

The Examiner asserts that Huang provides the skilled person to identify compounds that interfere with or enhance the angiogenesis pathway, stating that Huang teaches that the tight controls on vascular growth in adult tissues can be breached in pathologic states such as cancer, arthritis, and diabetic retinopathy. However, Huang fails to provide the skilled person with motivation to identify compounds that modulate HPTPbeta activity and VEGFR2 activity, wherein the amino acid sequences of HPTPbeta and VEGFR2 are within the parameters established in Applicants' claims. Instead, Huang identifies for the skilled person a PTP that, itself, modulates VEGFR2. This failure to motivate is not remedied by combining the teachings of Thorpe.

The passage of Thorpe cited in the Office Action sets forth a series of leaps beginning with the disclosure of antibodies that are VEGF2-specific and arriving at a signal transduction cascade, which merely includes activation of phospholipase and a phosphokinase. This series, alone or in combination with Huang, falls short of motivating the skilled person to identify compounds that modulate HPTPbeta activity and VEGFR2 activity, wherein the amino acid sequences of HPTPbeta and VEGFR2 are within the parameters established in Applicants' claims. There is simply no motivation in either or both of the cited references to identify compounds that modulate HPTPbeta activity and VEGFR2 activity to determine their suitability for use in the treatment of angiogenesis mediated disorders. Nor does such motivation exist to conduct such a method with the added consideration of Tie-2 activity. As such, Applicants submit that the cited

references fail to establish a *prima facie* case of obviousness, and the rejection as applied is improper. Therefore, Applicants respectfully request that it be withdrawn.

Conclusion

This response represents an earnest effort to place the application in proper form and to distinguish the invention as now claimed from the applied references. In view of the foregoing, reconsideration of this application, entry of the amendments presented herein, and allowance of all pending Claims is respectfully requested.

Respectfully submitted,

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